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ning of each regular issue of the PCT Gazette.

(54) Title: PREVENTION AND TREATMENT OF SYNUCLEINOPATHIC DISEASE

(57) Abstract: The invention provides improved agents and methods for treatment of diseases associated with synucleinopathic diseases, including Lewy bodies of alpha-synuclein in the brain of a patient. Such methods entail administering agents that induce a beneficial immunogenic response against the Lewy body. The methods are particularly useful for prophylactic and therapeutic treatment of Parkinson's disease.

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International application No.

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A. CLASSIFICATION OF SUBJECT MATTER

IPC: A01N 37/18(2007.01); A61K 38/00(2007.01); C07K 2/00(2007.01); 4/00(2007.01); 5/00(2007.01); 14/00(2007.01); 17/00(2007.01)

USPC: 530/300,350; 514/2; 424/184.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 530/300, 350; 514/2; 424/184.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LIPPA et al. Antibodies to alpha-synuclein detect Lewy bodies in many Down's syndrome brains with Alzheimer's disease. Ann. Neurol. March 1999, Vol 45. No. 3, pages 353-357.	57, 59, 71-72
X	WAKABAYASHI K. NACP, a presynaptic protein, immunoreactivity in Lewy bodies in Parkinson's disease. Neurosci. Lett. December 1997, Vol 239. No. 1, pages 45-48.	57, 59, 71-72
X	IRIZARRY M.C. Nigral and cortical Lewy bodies and dystrophic nigral neurites in Parkinson's disease and cortical Lewy body disease contain alpha-synuclein immunoreactivity. J. Neuropathol. Exp. Neurol. April 1998, Vol 57. No. 4, pages 334-37.	57, 59, 71-72
X	WAKABAYASHI K. Alpha-synuclein immunoreactivity in glial cytoplasmic inclusions in multiple system atrophy. Neurosci. Lett. 1998, Vol 249, pages 180-182.	57, 59, 71-72
A	WO99/40191 A1 (DNAS OR GENES PARTICIPATING IN PARKINSON'S DISEASE) 12 August 1999 (12.08.1999), Abstract only (Japanese language document).	1, 3, 8-11, 13-14, 36-41, 45-57, 59, 62, 71-72

☒ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

Special categories of cited documents	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combinations being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"Z" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

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C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 2002/0151464 A1 (WOLOZIN et al) 17 October 2002 (17.10.2002), full document, particularly Example 9.	1, 3, 8-10, 13-14, 36-41, 45-57, 59, 62, 71-72 ----- 1, 3, 8-11, 13-14, 36-41, 45-57, 59, 62, 71-72
X --- Y	WO00/72876 A2 (NEURALAB LIMITED.) 07 December 2000 (07.12.2000), full document, particularly p. 114 and claims.	1, 3, 8-11, 13-14, 36-41, 45-57, 59, 62, 71-72 ----- 1, 3, 8-11, 13-14, 36-41, 45-57, 59, 62, 71-72
X --- Y	WO99/27944 A1 (ATHENA NEUROSCIENCES, INC.) 10 June 1999 (10.06.1999), sec full document.	1, 3, 8-11, 13-14, 36-41, 45-57, 59, 62, 71-72 ----- 1, 3, 8-11, 13-14, 36-41, 45-57, 59, 62, 71-72
X --- Y	US 6,504,080 B1 (VAN DER PUTTEN P.H.) 07 January 2003 (07.01.2003), sec full document.	1, 3, 8-11, 13-14, 36-41, 45-57, 59, 62, 71-72 ----- 1, 3, 8-11, 13-14, 36-41, 45-57, 59, 62, 71-72

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International application No.

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Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1,3,8-11,13,14,36-41,45-57,59,62,71 and 72

Remark on Protest

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☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

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BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1, 3, 8-11, 13-14, 36-41, 45-57, 59, 62, 71-72 in part drawn to a method of preventing or treating via technical feature alpha-synuclein.

Group II, claim(s) 1, 2, 17-29, 33-41, 45-56, 57-58, 62, 71-72 in part drawn to a method of preventing or treating via technical feature antibodies to alpha-synuclein.

Group III, claim(s) 1, 4, 8-10, 12, 15, 16, 36-41, 45-56, 57, 59, 60, 62, 71-72 in part drawn to a method of preventing or treating via technical feature immunogenic fragment of alpha-synuclein.

Group IV, claims 1, 4-5, 8-10, 12, 15, 16, 36-41, 45-56, 57, 59, 60, 62, 71-72 in part drawn to a method of preventing or treating via technical feature amino acids 35-65 of alpha synuclein.

Group V, claim(s) 1, 4, 6, 8-10, 12, 15, 16, 36-41, 45-56, 57, 59-60, 62, 71-72 in part drawn to a method of preventing or treating via technical feature alpha-synuclein fragment comprising amino acids 130-140.

Group VI, claim(s) 1, 4, 7-10, 12, 15-16, 36-41, 45-57, 59-60, 62, 71-72 in part drawn to a method of preventing or treating via technical feature alpha-synuclein C-terminal fragment.

Group VII, claim(s) 1, 8-10, 17-29, 30-41, 45-56 in part drawn to a method of preventing or treating via technical feature polynucleotide encoding antibody.

Group VIII, claim(s) 42-43, 45-56, 57, 62, 71-72 in part drawn to a method of preventing or treating via technical feature Abeta peptide or fragment.

Group IX, claim(s) 42, 44 45-56, 57, 58, 62, 71-72 in part drawn to a method of preventing or treating via technical feature antibodies to Abeta or antibody fragment.

Group X, claim(s) 57, 59, 62 in part drawn to a pharmaceutical composition to the extent of 6CHC-1 or immunogenic fragment.

Group XI, claim(s) 57, 59, 60-62, drawn in part to a pharmaceutical composition to the extent of NAC.

Group X, claim(s) 65 drawn to a method of screening an antibody via contact with neuronal cell.

Group XI, claim(s) 66 drawn to a method of screening and antibody via determining specific binding with peptide of at least five amino acids of alpha synuclein.

Group XII, claim(s) 67-70 drawn to a method of screening and agent via contacting with a transgenic.

The inventions listed as Groups I-VIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The special technical feature of claim 1, alpha synuclein is anticipated by prior art, see in particular Jensen et al., Biochem J., 1997 Apr 15;323 (Pt 2):539-46 which teaches technical features alpha-synuclein, beta-synuclein, NAC and Abeta as well as binding thereto. Thus the technical features are not a contribution over the prior art and unity is therefore lacking. Further, the subsequent inventions are each separable as they recite different technical feature agents that differ in structure and function. The methods are similarly separable as they are comprised of different

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technical feature reagents, steps, functions, outcomes and effects. Accordingly, the inventions are separable and lack unity. Claims 63-64 are not included as the claims are improperly multiple dependent claims.